Amend claim 9 as follows:

--9. (amended) The method according to claim 1, wherein said covalent connection of the probe ends is performed by enzymatic, ribozyme-mediated or chemical ligation.--

REMARKS

This application has been amended in a manner that is believed to place it in condition for allowance at the time of the next Official Action.

Claims 1-13 are pending in the present application. Claims 3, 4 and 9 have been amended to more particularly point out and distinctly claim the present invention.

In the outstanding Official Action, claims 3, 4 and 9 were rejected under 35 USC §112, second paragraph, for allegedly being indefinite. It is believed that the present amendment obviates this rejection.

Claims 3, 4 and 9 were rejected for reciting the phrase "preferably". However, the claims have been amended in a manner so that the phrase "preferably" is no longer recited. Thus, it is believed that claims 3, 4 and 9 are definite to one of ordinary skill in the art.

Claims 1, 5, 6 and 9-13 were rejected under 35 USC §102(b) as allegedly being anticipated by NILSSON et al. (Science, Vol. 265, pp. 2085-2088). This rejection is respectfully traversed.

Applicant respectfully submits that the outstanding Official Action fails to meet its burden in showing that the claimed invention has been anticipated by NILSSON et al. It is believed that the NILSSON et al. publication fails to disclose or suggest each and every recitation of the claimed invention.

The claimed invention relates to a padlock probe anchored to a solid phase to which a nucleic acid sequence to be analyzed is added. A detectable marker is linked to the padlock probe. The padlock probe may also contain a cleavable segment (see Figure 1).

A nucleic acid-containing sample can be added to the anchored probe and segment. The target sequence of the nucleic acid sequence is hybridized to the complementary end-segments of the padlock probe. The padlock probe becomes circularized through ligation of the ends. Those padlock probes which have not hybridized to a nucleic acid sequence are cleaved, in a way that the detectable marker is removed together with a dissociable segment. The dissociable segments can be removed by washing. On the solid phase, the padlock probes, which have interacted with the nucleic acid sequence from the sample, can easily be detected through analysis of the detectable marker.

In the NILSSON et al. publication, padlock probes are used for localization and detection of a specific segment of a single stranded DNA. A padlock probe is defined as an oligonucleotide probe for localized detection of specific nucleic

acids composed of two target-complementary end-segments. These target-complementary end-segments may be connected by a linker. The padlock probe may then be added to solid phase anchored single-stranded DNA.

However, the padlock probe does not have a cleavable function or dissociable detectable functions. The padlock probe is simply hybridized to and circularized on the segment of the single-stranded DNA of interest. This nucleic acid sequence can be elucidated by use of detectable markers linked to the padlock probe.

Upon carefully reviewing Figure 4, applicant believes that NILSSON et al. do not teach the claimed method wherein the probe is provided indirectly or directly with a solid phase anchor and with a cleavable and detectable function, or with a dissociable and detectable function. In fact, applicant notes that the Official Action fails to identify a probe that is capable of linking to a solid phase when the target has interacted with the probe. Rather, the Official Action generically cites to Figure 4. Moreover, applicant believes that NILSSON et al. fail to teach a method capable of detecting, quantifying, and distinguishing between one or several variants with regard to the target sequences in a sample (see present specification, page 4, lines 35-38).

As a result, it is believed that the Official Action fails to meets its burden in showing that the claimed invention

is anticipated by NILSSON et al. Moreover, it is believed that the teachings of NILSSON et al. fail to anticipate or render obvious the claimed invention.

In the outstanding Official Action, claims 2-4 were rejected under 35 USC §103(a) as allegedly being unpatentable over NILSSON et al. in view of URDEA et al. 5,124,246. This rejection is respectfully traversed.

Applicant respectfully submits that the URDEA et al. publication fails to remedy the deficiencies of NILSSON et al. URDEA et al. relates to amplifying the signal in biochemical assays by using linear or branched oligonucleotide multimers (see Abstract, page 2). Thus, it is believed that URDEA et al. fail to teach the claimed method. It is believed that the proposed combination of NILSSON et al. in view of URDEA et al. fails to render obvious the claimed invention.

In the outstanding Official Action, claims 7 and 8 were rejected under 35 USC §103(a) as allegedly being unpatentable over NILSSON et al. in view of BIRKENMEYER et al. 5,427,930. This rejection is respectfully traversed.

The BIRKENMEYER et al. publication is directed to the improvement of a ligase chain reaction assay. BIRKENMEYER et al. set out to accomplish this by selecting and using target sequences such that only a single type, or two types, of deoxyribonucleotide triphosphate(s) are required to fill double gaps (see Abstract, page 1). BIRKENMEYER et al. fail to even

mention or suggest the claimed method of detecting a target nucleic acid sequence in a sample by contacting the sample of the probe to hybridize the probe to the target sequence, and detecting the hybridized probe. Thus, it is believed that the teachings of BIRKENMEYER et al. fail to remedy the deficiencies of NILSSON et al. It is believed that the proposed combination fails to render obvious the claimed invention.

In view of the present amendment and the foregoing remarks, therefore, it is believed that this application is now in condition for allowance, with claims 1-13, as presented. Allowance and passage to issue on that basis are accordingly respectfully requested.

Attached hereto is a marked-up version showing the changes made to the claims. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

Respectfully submitted,

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By _____

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April 15, 2003

"VERSION WITH MARKINGS TO SHOW CHANGES MADE"

IN THE CLAIMS:

Claim 3 has been amended as follows:

--3. (amended) The method according to claim 1, wherein one or both of the probe ends have at least two branches, [preferably with differential sequence specificities,] and a detectable function is provided on each of the branches on one end part of the probe, the detectable functions [preferably] being different and distinguishable from each other.--

Claim 4 has been amended as follows:

--4. (amended) The method according to claim 3, wherein one probe end is linear and the other probe end is branched[, preferably bifurcated].--

Claim 9 has been amended as follows:

--9. (amended) The method according to claim 1, wherein said covalent connection of the probe ends is performed by enzymatic, ribozyme-mediated or chemical ligation[, preferably enzymatic ligation].--